



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Christian P. Larsen et al. **Examiner:** Not yet known
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Filed: January 25, 2002 **Docket No.:** D0136NP/30436.5
Title: METHODS OF INDUCING ORGAN TRANSPLANT TOLERANCE AND
CORRECTING HEMOGLOBINOPATHIES

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CERTIFICATE UNDER 37 CFR 1.8:

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on July 31, 2002.

Renato Marco P. Domingo
By: Renato Marco P. Domingo

INFORMATION DISCLOSURE STATEMENT (37 C.F.R. § 1.97(b)(3))

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- U.S. Patent No. 4,603,102 issued July 29, 1986 – **Exhibit 1**
- U.S. Patent No. 5,430,057 issued July 4, 1995 – **Exhibit 2**
- U.S. Patent No. 5,434,131 issued July 18, 1995 – **Exhibit 3**
- U.S. Patent No. 5,559,148 issued September 24, 1996 – **Exhibit 4**
- U.S. Patent No. 5,637,481 issued June 10, 1997 – **Exhibit 5**
- U.S. Patent No. 5,773,253 issued June 30, 1998 – **Exhibit 6**
- U.S. Patent No. 5,844,095 issued December 1, 1998 – **Exhibit 7**
- U.S. Patent No. 5,851,795 issued December 22, 1998 – **Exhibit 8**
- U.S. Patent No. 5,876,692 issued March 2, 1999 – **Exhibit 9**
- U.S. Patent No. 5,885,579 issued March 23, 1999 – **Exhibit 10**
- U.S. Patent No. 5,885,796 issued March 23, 1999 – **Exhibit 11**

- U.S. Patent No. 6,090,914 issued July 18, 2000 – **Exhibit 12**
- U.S. Patent No. 6,113,898 issued September 5, 2000 – **Exhibit 13**
- U.S. Patent No. 6,217,867 B1 issued April 17, 2001 – **Exhibit 14**
- International Publication No. WO96/23071 published August 1, 1996 – **Exhibit 15**
- Abrams, Judith R. et al., “Blockade of T Lymphocyte Costimulation with Cytotoxic T Lymphocyte- associated Antigen 4-Immunoglobulin (CTLA4Ig) Reverse the Cellular Pathology of Psoriatic plaques, Including the Activation of Keratinocytes, Dendritic Cells, and Endothelial Cells,” *Journal of Experimental Medicine*, 2000, 192:681-693 – **Exhibit 16**
- Adams, Andrew B. et al., “Costimulation Blockade, Busulfan, and Bone Marrow Promote Titratable Macrochimerism, Induce Transplantation Tolerance, and Correct Genetic Hemoglobinopathies with Minimal Myelosuppression,” *Journal of Immunology*, 2001, 167:1103-11 – **Exhibit 17**
- Ahmed, Rafi et al., “Selection of Genetic Variants of Lymphocytic Choriomeningitis Virus in Spleens of Persistently Infected Mice,” *Journal of Experimental Medicine*, 1984, 160:521-40 – **Exhibit 18**
- Andreasen, Susanne Ørding et al., “Surface marker abnormalities in myelodysplastic syndromes,” *Journal of Immunology*, 2000, 164:3689-97 – **Exhibit 19**
- Aruffo, S., Presentation of “Approaches to Immune Regulation” at BIO 2000 in Boston, Massachusetts, March 27, 2000 – **Exhibit 20**
- Basch, Ross S. et al., “Growth of Human Hematopoietic Cells in Immunodeficient Mice Conditioned with Cyclophosphamide and Busulfan,” *Stem Cells*, 1997, 15:314-23 – **Exhibit 21**
- Becker, J.C., Abstract and Presentation of “A multi-center, randomized, double-blind, placebo controlled study to evaluate the safety and preliminary clinical activity of multiple doses of CTLA4Ig and LEA29Y administration intravenously to subjects with rheumatoid arthritis,” presented at American College of Rheumatology Conference: “2001 Innovative Therapies in Autoimmune Diseases,” San Francisco, California, March 8, 2001 – **Exhibit 22**

- Bevers, Edouard M. et al., "Transmembrane Phospholipid Distribution in Blood Cells: Control Mechanisms and Pathophysiological Significance," *Biological Chemistry*, 1998, 379:973-86 – **Exhibit 23**
- Bill, Jerome et al., "The MHC Molecule I-E is Necessary but not Sufficient for the Clonal Deletion of V β 11-Bearing T Cells," *Journal of Experimental Medicine*, 1989, 169:1405-19 – **Exhibit 24**
- Billingham, R. E. et al., "'Actively Acquired Tolerance' of Foreign Cells," *Nature*, 1953, 172:603-6 – **Exhibit 25**
- Bratton, Donna L. et al., "Appearance of Phosphatidylserine on Apoptotic Cells Requires Calcium-mediated Nonspecific Flip-Flop and Is Enhanced by Loss of the Aminophospholipid Translocase," *Journal of Biological Chemistry*, 1997, 272:26159-65 – **Exhibit 26**
- Brodsky, Isadore et al., "The Role of Busulfan/Cyclophosphamide Regimens in Allogeneic and Autologous Bone Marrow Transplant," *Cancer Investigation*, 1989, 7:509-13 – **Exhibit 27**
- Butz, Eric A. and Michael J. Bevan, "Massive Expansion of Antigen-Specific CD8⁺ T Cells during an Acute Virus Infection," *Immunity*, 1998, 8:167-75 – **Exhibit 28**
- Byrn, Randal A. et al., "Characterization of In Vitro Inhibition of Human Immunodeficiency Virus by Purified Recombinant CD4," *Journal of Virology*, 1989, 63:4370-5 – **Exhibit 29**
- Champlin, Richard et al., "Reinventing bone marrow transplantation: reducing toxicity using nonmyeloablative, preparative regimens and induction of graft-versus-malignancy," *Current Opinion in Oncology*, 1999, 11:87-95 – **Exhibit 30**
- Christian, John A. et al., "Methodologic considerations for the use of canine in vivo aged biotinylated erythrocytes to study RBC senescence," *Experimental Hematology*, 1996, 24:82-8 – **Exhibit 31**
- Closse, Christèle et al., "Phosphatidylserine-related adhesion of human erythrocytes to vascular endothelium," *British Journal of Hematology*, 1999, 107:300-2 – **Exhibit 32**
- Craddock, Charles, "Nonmyeloablative stem cell transplants," *Current Opinion in Hematology*, 1999, 6:383-7 – **Exhibit 33**

- Dariavach, Piona et al., "Human Ig superfamily CTLA-4 gene: chromosomal localization and identity of protein sequence between murine and human CTLA-4 cytoplasmic domains," *European Journal of Immunology*, 1988, 18:1901-5 – **Exhibit 34**
- Dash, Bret et al., "Deletion of a single *N*-linked glycosylation site from the transmembrane envelope protein of human immunodeficiency virus type 1 stops cleavage and transport of gp160 preventing *env*-mediated fusion," *Journal of General Virology*, 1994, 75:1389-97 – **Exhibit 35**
- Durham, Megan M. et al., "Cutting Edge: Administration of Anti-CD40 Ligand and Donor Bone Marrow Leads to Hemopoietic Chimerism and Donor-Specific Tolerance Without Cytoablative Conditioning," *Journal of Immunology*, 2000, 165:1-4 – **Exhibit 36**
- Dyson, P. J. et al., "Genes encoding ligands for deletion of V β 11 T cells cosegregate with mammary tumour virus genomes," *Nature*, 1991, 349:531-2 – **Exhibit 37**
- Falk, Kirsten et al., "Both Human and Mouse Cells Expressing H-2K^b and Ovalbumin Process the Same Peptide, SIINFEKL," *Cellular Immunology*, 1993, 150:447-52 – **Exhibit 38**
- Flesher, Alan R., Presentation of 'Transgenic Production, A Comparative Study' at Bio 99 in Seattle, Washington, April 15, 1999 – **Exhibit 39**
- Frasch, S. Courtney et al., "Regulation of Phospholipid Scramblase Activity during Apoptosis and Cell Activation by Protein Kinase C δ ," *Journal of Biological Chemistry*, 2000, 275:23065-73 – **Exhibit 40**
- Fujikawa, Kiyomi et al., "Short Communications: Nuclear Localization and Transforming Activity of Human Papillomavirus Type 16 E7- β -Galactosidase Fusion Protein: Characterization of the Nuclear Localization Sequence," *Virology*, 1994, 204:789-93 – **Exhibit 41**
- Gandhi, Rajesh B. et al., Abstract and Presentation of "Physical and Chemical Characterization of BMS-224818, A Recombinant Fusion Protein," in San Francisco, California, *PharmSci Supplement*, November 18, 1998, 1:S-535 – **Exhibit 42**

- Gérard, C. et al., "Production and Characterization of Polyclonal Antibodies Recognizing the Intracytoplasmic Third Loop of the 5-Hydroxytryptamine Receptor," *Neuroscience*, 1994, 62:721-39 – **Exhibit 43**
- Greene, JoAnne L. et al., "Covalent Dimerization of CD28/CTLA-4 and Oligomerization of CD80/CD86 Regulate T Cell Costimulatory Interactions," *Journal of Biological Chemistry*, 1996, 271:26762-71 – **Exhibit 44**
- Greve, Kimberly F., "Capillary electrophoretic examination of underivatized oligosaccharide mixtures released from immunoglobulin G antibodies and CTLA4Ig fusion protein," *Journal of Chromatography*, 1996, 749:237-245 – **Exhibit 45**
- Handschumacher, Robert E., "Immunosuppressive Agents," *Goodman and Gilman's: The Pharmacological Basis of Therapeutics*, Pergamon Press, NY, 1990, 1264-76 – **Exhibit 46**
- Hansen, John A. et al., "Monoclonal Antibodies Identifying a Novel T-Cell Antigen and Ia Antigens of Human Lymphocytes," *Immunogenetics*, 1980, 10:247-60 – **Exhibit 47**
- Hathcock, Karen S. et al., "Identification of an Alternative CTLA-4 Ligand Costimulatory for T Cell Activation," *Science*, 1993, 262:905-911 – **Exhibit 48**
- Honey, Karen et al., "CD40 Ligand Blockade Induces CD4⁺ T Cell Tolerance and Linked Suppression," *Journal of Immunology*, 1999, 163:4805-10 – **Exhibit 49**
- Ikeda, Toshio et al., "Isolation of a cDNA encoding the chicken p508/p97 (Lyt-10) transcription factor," *Gene*, 1994, 138:193-6 – **Exhibit 50**
- Ildstad, Suzanne T. and David H. Sachs, "Reconstitution with syngeneic plus allogeneic or xenogeneic bone marrow leads to specific acceptance of allografts or xenografts," *Nature*, 1984, 307:168-70 – **Exhibit 51**
- Johnsson, Bo et al., "Immobilization of Proteins to a Carboxymethyl-dextran-Modified Gold Surface for Biospecific Interaction Analysis in Surface Plasmon Resonance Sensors," *Analytical Biochemistry*, 1991, 198:268-77 – **Exhibit 52**
- Joneckis, Christopher C. et al., "Integrin $\alpha_4\beta_1$ and Glycoprotein IV (CD36) Are Expressed on Circulating Reticulocytes in Sickle Cell Anemia," *Blood*, 1993, 82:3548-55 – **Exhibit 53**

- Jones, Nancy H. et al., "Isolation of complementary DNA clones encoding the human lymphocyte glycoprotein T1/Leu-1," *Nature*, 1986, 323:346-9 – **Exhibit 54**
- Khilko, Sergei N. et al., "Direct Detection of Major Histocompatibility Complex Class I Binding to Antigenic Peptides Using Surface Plasmon Resonance," *Journal of Biological Chemistry*, 1993, 268:15425-34 – **Exhibit 55**
- Knoerzer, Debbie Barney et al., "Collagen-induced Arthritis in the BB Rat: Prevention of Disease by Treatment with CTLA-4-Ig," *Journal of Clinical Investigation*, 1995, 96:987-93 – **Exhibit 56**
- Kolhekar, Aparna S. et al., "Peptidylglycine α -Hydroxylating Monooxygenase: Active Site Residues, Disulfide Linkages, and a Two-Domain Model of the Catalytic Core," *Biochemistry*, 1997, 36:10901-9 – **Exhibit 57**
- Krishnamurti, Lashmanan et al., "Bone Marrow Transplantation without Myeloablation for Sickle Cell Disease," *New England Journal of Medicine*, 2001, 344:68 – **Exhibit 58**
- Kuypers, Frans A. et al., "Detection of Altered Membrane Phospholipid Asymmetry in Subpopulations of Human Red Blood Cells Using Fluorescently Labeled Annexin V," *Blood*, 1996, 87:1179-87 – **Exhibit 59**
- Larsen, Christian P., Presentation of "Costimulation blockade: Progress toward clinical application" at the American Society of Transplantation Meeting in Las Croabas, Puerto Rico, Jan. 13-17, 2000 – **Exhibit 60**
- Larsen, Christian P., Presentation of "Costimulation blockade: progress toward clinical application" at Canadian Society of Transplantation Annual Scientific meeting in Mont Tremblant, Quebec, Canada, March 3-4, 2000 – **Exhibit 61**
- Larsen, Christian P. et al., Abstract of "Prolongation of Renal Allograft Survival with Blockade of the CD28 Pathway Using A Novel Mutant CTLA4-IG Fusion Protein In Non-Human Primates," in *Transplantation*, 2000, 69:S123, #45 – **Exhibit 62**
- Larsen, Christian P. et al., Presentation of "Prolongation of Renal Allograft Survival With Blockade of the CD28 Pathway Using A Novel Mutant CTLA4-Ig Protein In Nonhuman

Primates” at the American Society of Transplantation Meeting in Chicago, Illinois, March 3-4, 2000— **Exhibit 63**

- Larsen, Christian P., Presentation of “Manipulation of Costimulatory Pathways: Targeting CD80 and CD86” at the XVII congress of the Transplantation Society in Rome, Italy, Aug. 27-Sept.1, 2000 – **Exhibit 64**
- Lasky, Laurence A. et al., “Neutralization of the AIDS Retrovirus by Antibodies to a Recombinant Envelope Glycoprotein,” *Science*, 1986, 233:209-12 – **Exhibit 65**
- Lenz, Laurel L. et al., “Requirements for Bone Marrow-derived Antigen-presenting Cells in Priming Cytotoxic T Cell Responses to Intracellular Pathogens,” *Journal of Experimental Medicine*, 2000, 192:1135-42 – **Exhibit 66**
- Linsley, Peter S. et al., “Coexpression and Functional Cooperation of CTLA-4 and CD28 on Activated T Lymphocytes,” *Journal of Experimental Medicine*, 1992, 176:1595-604 – **Exhibit 67**
- Linsley, Peter S. et al., “Human B7-1 (CD80) and B7-2 (CD86) Bind with Similar Avidities but Distinct Kinetics to CD28 and CTLA-4 Receptors,” *Immunity*, 1994, 1:793-801 – **Exhibit 68**
- Linsley, Peter S. et al., “Binding Stoichiometry of the Cytotoxic T Lymphocyte-associated Molecule-4 (CTLA-4),” *Journal of Biological Chemistry*, 1995, 270:15417-24 – **Exhibit 69**
- Lucarelli, G. et al., “Marrow Transplantation for Thalassemia after Treatment with Busulfan and Cyclophosphamide,” *Annals New York Academy of Sciences*, 1985, 445:428-31 – **Exhibit 70**
- Lyons, A. Bruce and Christopher R. Parish, “Determination of lymphocyte division by flow cytometry,” *Journal of Immunological Methods*, 1994, 171:131-7 – **Exhibit 71**
- Maini, Ravinder et al., “Infliximab (chimeric anti-tumour necrosis factor α monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomized phase III trial,” *The Lancet*, 1999, 354:1932-9 – **Exhibit 72**

- Malik, Najma et al., "Molecular Cloning, Sequence Analysis, and Functional Expression of a Novel Growth Regulator, Oncostatin M," *Molecular and Cellular Biology*, 1989, 9:2847-53 – **Exhibit 73**
- Markees, Thomas G. et al., "Long-Term Survival of Skin Allografts Induced by Donor Splenocytes and Anti-CD154 Antibody in Thymectomized Mice Requires CD4⁺ T Cells, Interferon- γ , and CTLA4," *Journal of Clinical Investigation*, 1998, 101:2446-55 – **Exhibit 74**
- Martin, Paul J. et al., "Preincubation of Donor Bone Marrow Cells with a Combination of Murine Monoclonal Anti-T-Cell Antibodies Without Complement Does Not Prevent Graft-Versus-Host Disease After Allogeneic Marrow Transplantation," *Journal of Clinical Immunology*, 1984, 4:18-22 – **Exhibit 75**
- Mathiesen, T. et al., "Prolonged survival and vascularization of xenografted human glioblastoma cells in the central nervous system of Cyclosporine A treated rats," *Cancer Letters*, 1989, 44:151-6 – **Exhibit 76**
- Mayumi, Hisanori and Robert A. Good, "Long-Lasting Skin Allograft Tolerance in Adult Mice Induced Across Fully Allogeneic (Multimajor H-2 Plus Multiminor Histocompatibility) Antigen Barriers by a Tolerance-Inducing Method Using Cyclophosphamide," *Journal of Experimental Medicine*, 1989, 169:213-38 – **Exhibit 77**
- Mentzer, William C. and Morton J. Cowan, "Bone Marrow Transplantation for β -Thalassemia: The University of California San Francisco Experience," *Journal of Pediatric Hematology/Oncology*, 2000, 22:598-601 – **Exhibit 78**
- Metzler, William J. et al., "Solution structure of human CTLA-4 and delineation of a CD80/CD86 binding site conserved in CD28," *Nature Structural Biology*, 1997, 4:527-31 – **Exhibit 79**
- Moreland, Larry W. et al., "Etanercept Therapy in Rheumatoid Arthritis: A Randomized, Controlled Trial," *Annals of Internal Medicine*, 1999, 130:478-86 – **Exhibit 80**
- Murali-Krishna, Kaja et al., "Counting Antigen-Specific CD8 T Cells: A Reevaluation of Bystander Activation during Viral Infection", *Immunity*, 1998, 8:177-87 – **Exhibit 81**

- Murali-Krishna and Rafi Ahmed, "Cutting Edge: Naïve T Cells Masquerading as Memory Cells," *Journal of Immunology*, 2000, 165:1733-7 – **Exhibit 82**
- O'Shannessy, Daniel J. et al., "Determination of Rate and Equilibrium Binding Constants for Macromolecular Interactions Using Surface Plasmon Resonance: Use of Nonlinear Least Squares Analysis Methods," *Analytical Biochemistry*, 1993, 212:457-68 – **Exhibit 83**
- Oaks, Martin K. et al., "A Native Soluble Form of CTLA-4," *Cellular Immunology*, 2000, 201:144-53 – **Exhibit 84**
- Owen, Ray D., "Immunogenetic Consequences of Vascular Anastomoses between bovine twins," *Science*, 1945, 102:400-1 – **Exhibit 85**
- Pászty, Chris et al., "Transgenic Knockout Mice with Exclusively Human Sick Cell Hemoglobin and Sick Cell Disease," *Science*, 1997, 278:876-8 – **Exhibit 86**
- Peach, Robert J. et al., "Complementarity Determining Region 1 (CDR-1)- and CDR3-analogous Regions in CTLA-4 and CD28 Determine the Binding to B7-1," *Journal of Experimental Medicine*, 1994, 180:2049-58 – **Exhibit 87**
- Pearson, Thomas C. et al., "CTLA4-Ig Plus Bone Marrow Induces Long-Term Allograft Survival and Donor-Specific Unresponsiveness in the Murine Model," *Transplantation*, 1996, 61:997-1004 – **Exhibit 88**
- Pichlmayr, R. et al., "Placebo-controlled study of mycophenolate mofetil combined with cyclosporin and corticosteroids for prevention of acute rejection," *The Lancet*, 1995, 345:1321-5 – **Exhibit 89**
- Platt, Ora H. and Eva C. Guinan, "Bone Marrow Transplantation in Sick Cell Anemia – The Dilemma of Choice," *New England Journal of Medicine*, 1996, 335:426-8 – **Exhibit 90**
- Ruedl, Christiane et al., "Phenotypic and functional characterization of CD11c⁺ dendritic cell population in mouse Peyer's patches," *European Journal of Immunology*, 1996, 26:1801-6 – **Exhibit 91**
- Salomon, Benoît and Jeffrey A. Bluestone, "Complexities of CD28/B7: CTLA-4 Costimulatory Pathways in Autoimmunity and Transplantation," *Annual Review of Immunology*, 2001, 19:225-52 – **Exhibit 92**

- Santos, G. W. et al., "HLA-Identical Marrow Transplants in Aplastic Anemia, Acute Leukemia, and Lymphosarcoma Employing Cyclophosphamide," *Human Bone Marrow Transplantation*, 1976, 63-9 – **Exhibit 93**
- Sayegh, Mohamed H. et al., "Donor Antigen is Necessary for the Prevention of Chronic Rejection in CTLA4Ig-Treated Murine Cardiac Allograft Recipients," *Transplantation*, 1997, 64:1646-50 – **Exhibit 94**
- Serke, Stefan and Dieter Huhn, "Identification of CD71 (transferring receptor) expressing erythrocytes by multiparameter-flow-cytometry (MP-FCM): correlation to the quantitation of reticulocytes as determined by conventional microscopy and by MP-FCM using a RNA-staining dye," *British Journal of Hematology*, 1992, 81:432-9 – **Exhibit 95**
- Sfrikakis, Peter P. et al., "CD28 Expression On T Cell Subsets In Vivo and CD28-Mediated T Cell Response In Vitro in Patients with Rheumatoid Arthritis," *Arthritis & Rheumatism*, 1995, 38:649-54 – **Exhibit 96**
- Shahinian, Arda et al., "Differential T Cell Costimulatory Requirements in CD28-Deficient Mice," *Science*, 1993, 261:609-12 – **Exhibit 97**
- Sharabi, Yedida and David H. Sachs, "Mixed Chimerism and Permanent Specific Transplantation Tolerance Induced by a Nonlethal Preparative Regimen," *Journal of Experimental Medicine*, 1989, 169:493-502 – **Exhibit 98**
- Shehee, W. Ronald et al., "Lethal thalassemia after insertional disruption of the mouse major adult β -globin gene," *Proceedings of the National Academy of Sciences of the United States of America*, 1993, 90:3177-81 – **Exhibit 99**
- Slavin, Shimon et al., "Nonmyeloablative Stem Cell Transplantation and Cell Therapy as an Alternative to Conventional Bone Marrow Transplantation with Lethal Cytoablation for the Treatment of Malignant and Nonmalignant Hematologic Diseases," *Blood*, 1998, 91:756-63
Exhibit 100
- Smith, Douglas H. et al., "Blocking of HIV-1 Infectivity by a Soluble, Secreted Form of the CD4 Antigen," *Science*, 1987, 238:1704-7 – **Exhibit 101**

- Spitzer, Thomas R. et al., "Intentional Induction of Mixed Chimerism and Achievement of Antitumor Responses After Nonmyeloablative Conditioning Therapy and HLA-Matched Donor Bone Marrow Transplantation for Refractory Hematologic Malignancies," *Biology of Blood and Marrow Transplantation*, 2000, 6:309-20 – **Exhibit 102**
- Srinivas, N. R. et al., "Pharmacokinetics and Pharmacodynamics of CTLA4Ig (BMS-188667), a Novel Immunosuppressive Agent, in Monkeys following Multiple Doses," *Journal of Pharmaceutical Sciences*, 1996, 85:1-4 – **Exhibit 103**
- Srinivas, Nuggehally R. et al., "Assessment of Dose Proportionality, Absolute Bioavailability, and Immunogenicity Response of CTLA4Ig (BMS-188667), a Novel Immunosuppressive Agent, Following Subcutaneous and Intravenous Administration to Rats," *Pharmaceutical Research*, 1997, 14:911-6 – **Exhibit 104**
- Swerlick, Robert A. et al., " $\alpha_4\beta_1$ -Integrin Expression on Sickle Reticulocytes: Vascular Cell Adhesion Molecule-1-Dependent Binding to Endothelium," *Blood*, 1993, 82:1891-9 – **Exhibit 105**
- Sykes, Megan et al., "Induction of high levels of allogeneic hematopoietic reconstitution and donor-specific tolerance without myelosuppressive conditioning," *Nature Medicine*, 1997, 3:783-7 – **Exhibit 106**
- Thomas, E. Donnall et al., "Marrow Transplantation for Thalassaemia," *The Lancet*, 1982, 2:227-9 – **Exhibit 107**
- Tomita, Yukihiro et al., "Myelosuppressive Condition Is Required to Achieve Engraftment of Pluripotent Stem Cells Contained in Moderate Doses of Syngeneic Bone Marrow," *Blood*, 1994, 83:939-48 – **Exhibit 108**
- Tomita, Yukihiro et al., "Role of Intrathymic Clonal Deletion and Peripheral Anergy in Transplantation Tolerance Induced by Bone Marrow Transplantation in Mice Conditioned with a Nonmyeloablative Regimen," *Journal of Immunology*, 1994, 153:1087-98 – **Exhibit 109**
- Turgeon, Nicole A. et al., "Viral Infection Abrogates CD8⁺ T-cell Deletion Induced by Costimulation Blockade," *Journal of Surgical Research*, 2000, 93:63-9 – **Exhibit 110**

- Urlaub, Gail et al., "Effect of Gamma Rays at the Dihydrofolate Reductase Locus: Deletions and Inversions," *Somatic Cell and Molecular Genetics*, 1986, 12:555-66 – **Exhibit 111**
- Vermes, István et al., "A novel assay for apoptosis Flow cytometric detection of phosphatidylserine expression on early apoptotic cells using fluorescein labelled Annexin V," *Journal of Immunological Methods*, 1995, 184:39-51 – **Exhibit 112**
- Vermylen, C. et al., "Haematopoietic stem cell transplantation for sickle cell anaemia: the first 50 patients transplanted in Belgium," *Bone Marrow Transplantation*, 1998, 22:1-6 – **Exhibit 113**
- Walters, Mark C. et al., "Impact of bone marrow transplantation for symptomatic sickle cell disease: an interim report," *Blood*, 2000, 95:1918-24 – **Exhibit 114**
- Warner, G. L. et al., Abstract and Presentation of "Bioactivity of BMS-188667 (CTLA4Ig) in Cynomolgus Monkeys," in Seattle, Washington, March 16-22, 1995 – **Exhibit 115**
- Webb, Louise M. C. et al., "Prevention and amelioration of collagen-induced arthritis by blockade of the CD28 co-stimulatory pathway: requirement for both B7-1 and B7-2" *European Journal of Immunology*, 1996, 26:2320-8 – **Exhibit 116**
- Weinblatt, Michael E. et al., "A Trial of Etanercept, A Recombinant Tumor Necrosis Factor Receptor: Fc Fusion Protein, in Patients with Rheumatoid Arthritis Receiving Methotrexate," *New England Journal of Medicine*, 1999, 340:253-9 – **Exhibit 117**
- Weiner, R. et al., Abstract and Presentation of "Validation and PK Application of a Double Antibody Sandwich Enzyme Immunoassay For the Quantitation of Human CTLA4Ig Fusion Protein (BMS-188667) in Mouse Serum," November 6-10, 1994 – **Exhibit 118**
- Weiner, Russell et al., Abstract and Presentation of "Validation of an Enzyme Immunoassay for the Quantitation of Human CTLA4Ig Fusion Protein in Human Serum," in Miami, Florida, November 1995 – **Exhibit 119**
- Weiner, Russell, Abstract and Presentation of "Automation and Validation of An EIA For Quantitation of Human CTLA4Ig in Monkey Serum," in Miami, Florida, November 1995 – **Exhibit 120**

- Weiner, Russell S. et al., "A sensitive enzyme immunoassay for the quantitation of human CTLA4Ig fusion protein in mouse serum: pharmacokinetic application to optimizing cell line selection," *Journal of Pharmaceutical and Biomedical Analysis*, 1997, 15:571-579 – **Exhibit 121**
- Weiner, Russell S., Abstract and Presentation of "Industrial Perspectives of Primary Analytical Tools for Macromolecules- Principles and Applications with Examples" March 1, 2000 – **Exhibit 122**
- Wekerle, Thomas et al., "Extrathymic T Cell Deletion and Allogeneic Stem Cell Engraftment Induced with Costimulatory Blockade Is Followed by Central T Cell Tolerance," *Journal of Experimental Medicine*, 1998, 187:2037-44 – **Exhibit 123**
- Wekerle, Thomas et al., "Allogeneic bone marrow transplantation with co-stimulatory blockade induces macrochimerism and tolerance without cytoreductive host treatment," *Nature Medicine*, 2000, 6:464-9 – **Exhibit 124**
- Wells, Andrew D. et al., "Following the Fate of Individual T Cells throughout Activation and Clonal Expansion," *Journal of Clinical Investigation*, 100:3173-83 – **Exhibit 125**
- Welsh, Raymond M. et al., "Virus-Induced Abrogation of Transplantation Tolerance Induced by Donor-Specific Transfusion and Anti-CD154 Antibody," *Journal of Virology*, 2000, 74:2210-8 – **Exhibit 126**
- Whitmire, Jason K. et al., "CD40 Ligand-Deficient Mice Generate a Normal Primary Cytotoxic T-Lymphocyte Response but a Defective Humoral Response to a Viral Infection," *Journal of Virology*, 1996, 70:8375-81 – **Exhibit 127**
- Whitmire, Jason K. et al., "CD40-CD40 Ligand Costimulation is Required for Generating Antiviral CD4 T Cell Responses But Is Dispensable for CD8 T Cell Responses," *Journal of Immunology*, 1999, 163:3194-201 – **Exhibit 128**
- Whitney, J. Barry III, "Simplified Typing of Mouse Hemoglobin (*Hbb*) Phenotypes Using Cystamine," *Biochemical Genetics*, 1978, 16:667-72 – **Exhibit 129**

- Williams, Matthew A. et al., "Genetic Characterization of Strain Differences in the Ability to Mediate CD40/CD28-Independent Rejection of Skin Allografts," *Journal of Immunology*, 2000, 165:6849-57 – **Exhibit 130**
- Wood, Brent L. et al., "Increased Erythrocyte Phosphatidylserine Exposure in Sick Cell Disease: Flow-Cytometric Measurement and Clinical Associations," *Blood*, 1996, 88:1873-80 – **Exhibit 131**
- Yang, Hyekyung and Raymond M. Welsh, "Induction of Alloreactive Cytotoxic T Cells by Acute Virus Infection of Mice," *Journal of Immunology*, 1986, 136:1186-93 – **Exhibit 132**
- Yang, Hyekyung et al., "Virus-Induced Polyclonal Cytotoxic T Lymphocyte Stimulation," *Journal of Immunology*, 1989, 142:1710-8 – **Exhibit 133**
- Yeager, A. M. et al., "Growth retardation and depigmentation of hair after high-dose busulfan and congenic hemtopoietic cell transplantation in mice," *Bone Marrow Transplantation*, 1992, 9:199-204 – **Exhibit 134**
- Yokochi, Takashi et al, "B Lymphoblast Antigen (BB-1) Expressed on Epstein-Barr Virus-Activated B Cell Blasts, B Lymphoblastoid Cell Lines, And Burkitt's Lymphomas," *Journal of Immunology*, 1982, 128:823-7 – **Exhibit 135**
- Zarozinski, Christopher C. and Raymond M. Welsh, "Minimal Bystander Activation of CD8 T Cells during the Virus-induced Polyclonal T Cell Response," *Journal of Experimental Medicine*, 1997, 185:1629-39 – **Exhibit 136**

This statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(a)(2), copies of each document or other information listed on the enclosed Form 1449 are provided.

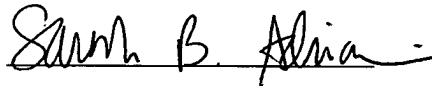
No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that the

references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. § 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

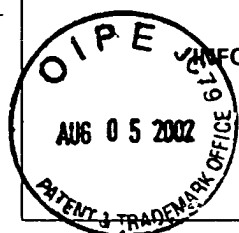
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Sarah B. Adriano", with a horizontal line drawn underneath the signature.

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FORM 1449*



INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION

(Use several sheets if necessary)

Docket Number

D0136NP/30436.58USU1

Application Number

10/057,288

Applicant

Christian P. Larsen et al.

Filing Date

January 25, 2002

Group Art Unit

1646

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	4,603,102 (Exhibit 1)	07/29/86	Himmelman et al.			06/26/85
	5,430,057 (Exhibit 2)	07/04/95	Andersson et al.			09/30/93
	5,434,131 (Exhibit 3)	07/18/95	Linsley et al.			05/26/93
	5,559,148 (Exhibit 4)	09/24/96	Andersson et al.			05/24/95
	5,637,481 (Exhibit 5)	06/10/97	Ledbetter et al.			09/13/93
	5,773,253 (Exhibit 6)	06/30/98	Linsley et al.			07/21/95
	5,844,095 (Exhibit 7)	12/01/98	Linsley et al.			01/18/95
	5,851,795 (Exhibit 8)	12/22/98	Linsley et al.			06/02/95
	5,876,692 (Exhibit 9)	03/02/99	Ildstad			01/17/97
	5,885,579 (Exhibit 10)	03/23/99	Linsley et al.			07/08/97
	5,885,796 (Exhibit 11)	03/23/99	Linsley et al.			06/05/95
	6,090,914 (Exhibit 12)	07/18/00	Linsley et al.			04/15/94
	6,113,898 (Exhibit 13)	09/05/00	Anderson et al.			06/07/95
	6,217,867 B1 (Exhibit 14)	04/17/01	Ildstad			10/22/98

FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO96/23071 (Exhibit 15)	08/01/96	PCT				X

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Abrams, Judith R. et al., "Blockade of T Lymphocyte Costimulation with Cytotoxic T Lymphocyte-associated Antigen 4-Immunoglobulin (CTLA4Ig) Reverse the Cellular Pathology of Psoriatic plaques, Including the Activation of Keratinocytes, Dendritic Cells, and Endothelial Cells," <i>Journal of Experimental Medicine</i> , 2000, 192:681-693 (Exhibit 16)
	Adams, Andrew B. et al., "Costimulation Blockade, Busulfan, and Bone Marrow Promote Titratable Macrochimerism, Induce Transplantation Tolerance, and Correct Genetic Hemoglobinopathies with Minimal Myelosuppression," <i>Journal of Immunology</i> , 2001, 167:1103-11 (Exhibit 17)
	Ahmed, Rafi et al., "Selection of Genetic Variants of Lymphocytic Choriomeningitis Virus in Spleens of Persistently Infected Mice," <i>Journal of Experimental Medicine</i> , 1984, 160:521-40 (Exhibit 18)

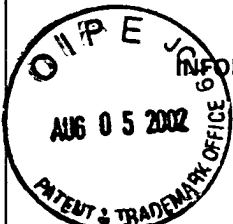
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*Substitute Disclosure Statement Form (PTO-1449)

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FORM 1449*  INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number D0136NP/30436.58USU1	Application Number 10/057,288
	Applicant Christian P. Larsen et al.	
	Filing Date January 25, 2002	Group Art Unit 1646

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
		Andreasen, Susanne Ørding et al., "Surface marker abnormalities in myelodysplastic syndromes," <i>Journal of Immunology</i> , 2000, 164:3689-97 (Exhibit 19)
		Aruffo, S., Presentation of "Approaches to Immune Regulation" at BIO 2000 in Boston, Massachusetts, March 27, 2000 (Exhibit 20)
		Basch, Ross S. et al., "Growth of Human Hematopoietic Cells in Immunodeficient Mice Conditioned with Cyclophosphamide and Busulfan," <i>Stem Cells</i> , 1997, 15:314-23 (Exhibit 21)
		Becker, J.C., Abstract and Presentation of "A multi-center, randomized, double-blind, placebo controlled study to evaluate the safety and preliminary clinical activity of multiple doses of CTLA4Ig and LEA29Y administration intravenously to subjects with rheumatoid arthritis," presented at American College of Rheumatology Conference: "2001 Innovative Therapies in Autoimmune Diseases," San Francisco, California, March 8, 2001 (Exhibit 22)
		Beyers, Edouard M. et al., "Transmembrane Phospholipid Distribution in Blood Cells: Control Mechanisms and Pathophysiological Significance," <i>Biological Chemistry</i> , 1998, 379:973-86 (Exhibit 23)
		Bill, Jerome et al., "The MHC Molecule I-E is Necessary but not Sufficient for the Clonal Deletion of Vβ11-Bearing T Cells," <i>Journal of Experimental Medicine</i> , 1989, 169:1405-19 (Exhibit 24)
		Billingham, R. E. et al., "'Actively Acquired Tolerance' of Foreign Cells," <i>Nature</i> , 1953, 172:603-6 (Exhibit 25)
		Bratton, Donna L. et al., "Appearance of Phosphatidylserine on Apoptotic Cells Requires Calcium-mediated Nonspecific Flip-Flop and Is Enhanced by Loss of the Aminophospholipid Translocase," <i>Journal of Biological Chemistry</i> , 1997, 272:26159-65 (Exhibit 26)
		Brodsky, Isadore et al., "The Role of Busulfan/Cyclophosphamide Regimens in Allogeneic and Autologous Bone Marrow Transplant," <i>Cancer Investigation</i> , 1989, 7:509-13 (Exhibit 27)
		Butz, Eric A. and Michael J. Bevan, "Massive Expansion of Antigen-Specific CD8 ⁺ T Cells during an Acute Virus Infection," <i>Immunity</i> , 1998, 8:167-75 (Exhibit 28)
		Byrn, Randal A. et al., "Characterization of In Vitro Inhibition of Human Immunodeficiency Virus by Purified Recombinant CD4," <i>Journal of Virology</i> , 1989, 63:4370-5 (Exhibit 29)
		Champlin, Richard et al., "Reinventing bone marrow transplantation: reducing toxicity using nonmyeloablative, preparative regimens and induction of graft-versus-malignancy," <i>Current Opinion in Oncology</i> , 1999, 11:87-95 (Exhibit 30)
		Christian, John A. et al., "Methodologic considerations for the use of canine in vivo aged biotinylated erythrocytes to study RBC senescence," <i>Experimental Hematology</i> , 1996, 24:82-8 (Exhibit 31)
		Closse, Christèle et al., "Phosphatidylserine-related adhesion of human erythrocytes to vascular endothelium," <i>British Journal of Hematology</i> , 1999, 107:300-2 (Exhibit 32)
		Craddock, Charles, "Nonmyeloablative stem cell transplants," <i>Current Opinion in Hematology</i> , 1999, 6:383-7 (Exhibit 33)
		Dariavach, Piona et al., "Human Ig superfamily CTLA-4 gene: chromosomal localization and identity of protein sequence between murine and human CTLA-4 cytoplasmic domains," <i>European Journal of Immunology</i> , 1988, 18:1901-5 (Exhibit 34)

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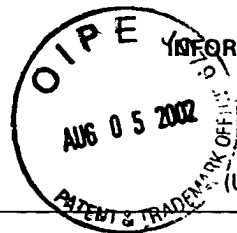
	Dash, Bret et al., "Deletion of a single N-linked glycosylation site from the transmembrane envelope protein of human immunodeficiency virus type 1 stops cleavage and transport of gp160 preventing env-mediated fusion," <i>Journal of General Virology</i> , 1994, 75:1389-97 (Exhibit 35)
	Durham, Megan M. et al., "Cutting Edge: Administration of Anti-CD40 Ligand and Donor Bone Marrow Leads to Hemopoietic Chimerism and Donor-Specific Tolerance Without Cytoinductive Conditioning," <i>Journal of Immunology</i> , 2000, 165:1-4 (Exhibit 36)
	Dyson, P. J. et al., "Genes encoding ligands for deletion of Vβ11 T cells cosegregate with mammary tumour virus genomes," <i>Nature</i> , 1991, 349:531-2 (Exhibit 37)
	Falk, Kirsten et al., "Both Human and Mouse Cells Expressing H-2K ^b and Ovalbumin Process the Same Peptide, SIINFEKL," <i>Cellular Immunology</i> , 1993, 150:447-52 (Exhibit 38)
	Flesher, Alan R., Presentation of 'Transgenic Production, A Comparative Study' at Bio 99 in Seattle, Washington, April 15, 1999 (Exhibit 39)
	Frasch, S. Courtney et al., "Regulation of Phospholipid Scramblase Activity during Apoptosis and Cell Activation by Protein Kinase Cδ," <i>Journal of Biological Chemistry</i> , 2000, 275:23065-73 (Exhibit 40)
	Fujikawa, Kiyomi et al., "Short Communications: Nuclear Localization and Transforming Activity of Human Papillomavirus Type 16 E7-β-Galactosidase Fusion Protein: Characterization of the Nuclear Localization Sequence," <i>Virology</i> , 1994, 204:789-93 (Exhibit 41)
	Gandhi, Rajesh B. et al., Abstract and Presentation of "Physical and Chemical Characterization of BMS-224818, A Recombinant Fusion Protein," in San Francisco, California, <i>PharmSci Supplement</i> , November 18, 1998, 1:S-535 (Exhibit 42)
	Gérard, C. et al., "Production and Characterization of Polyclonal Antibodies Recognizing the Intracytoplasmic Third Loop of the 5-Hydroxytryptamine Receptor," <i>Neuroscience</i> , 1994, 62:721-39 (Exhibit 43)
	Greene, JoAnne L. et al., "Covalent Dimerization of CD28/CTLA-4 and Oligomerization of CD80/CD86 Regulate T Cell Costimulatory Interactions," <i>Journal of Biological Chemistry</i> , 1996, 271:26762-71 (Exhibit 44)
	Greve, Kimberly F., "Capillary electrophoretic examination of underivatized oligosaccharide mixtures released from immunoglobulin G antibodies and CTLA4lg fusion protein," <i>Journal of Chromatography</i> , 1996, 749:237-245 (Exhibit 45)
	Handschumacher, Robert E., "Immunosuppressive Agents," <i>Goodman and Gilman's: The Pharmacological Basis of Therapeutics</i> , Pergamon Press, NY, 1990, 1264-76 (Exhibit 46)
	Hansen, John A. et al., "Monoclonal Antibodies Identifying a Novel T-Cell Antigen and Ia Antigens of Human Lymphocytes," <i>Immunogenetics</i> , 1980, 10:247-60 (Exhibit 47)
	Hathcock, Karen S. et al., "Identification of an Alternative CTLA-4 Ligand Costimulatory for T Cell Activation," <i>Science</i> , 1993, 262:905-911 (Exhibit 48)
	Honey, Karen et al., "CD40 Ligand Blockade Induces CD4 ⁺ T Cell Tolerance and Linked Suppression," <i>Journal of Immunology</i> , 1999, 163:4805-10 (Exhibit 49)
	Ikedo, Toshio et al., "Isolation of a cDNA encoding the chicken p508/p97 (Lyt-10) transcription factor," <i>Gene</i> , 1994, 138:193-6 (Exhibit 50)

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FORM 1449*



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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Ildstad, Suzanne T. and David H. Sachs, "Reconstitution with syngeneic plus allogeneic or xenogeneic bone marrow leads to specific acceptance of allografts or xenografts," <i>Nature</i> , 1984, 307:168-70 (Exhibit 51)
	Johnsson, Bo et al., "Immobilization of Proteins to a Carboxymethyl-dextran-Modified Gold Surface for Biospecific Interaction Analysis in Surface Plasmon Resonance Sensors," <i>Analytical Biochemistry</i> , 1991, 198:268-77 (Exhibit 52)
	Joneckis, Christopher C. et al., "Integrin $\alpha 4 \beta 1$ and Glycoprotein IV (CD36) Are Expressed on Circulating Reticulocytes in Sickle Cell Anemia," <i>Blood</i> , 1993, 82:3548-55 (Exhibit 53)
	Jones, Nancy H. et al., "Isolation of complementary DNA clones encoding the human lymphocyte glycoprotein T1/Leu-1," <i>Nature</i> , 1986, 323:346-9 (Exhibit 54)
	Khilko, Sergei N. et al., "Direct Detection of Major Histocompatibility Complex Class I Binding to Antigenic Peptides Using Surface Plasmon Resonance," <i>Journal of Biological Chemistry</i> , 1993, 268:15425-34 (Exhibit 55)
	Knoerzer, Debbie Barney et al., "Collagen-induced Arthritis in the BB Rat: Prevention of Disease by Treatment with CTLA-4-Ig," <i>Journal of Clinical Investigation</i> , 1995, 96:987-93 (Exhibit 56)
	Kolhekar, Aparna S. et al., "Peptidylglycine α -Hydroxylating Monooxygenase: Active Site Residues, Disulfide Linkages, and a Two-Domain Model of the Catalytic Core," <i>Biochemistry</i> , 1997, 36:10901-9 (Exhibit 57)
	Krishnamurti, Lashmanan et al., "Bone Marrow Transplantation without Myeloablation for Sickle Cell Disease," <i>New England Journal of Medicine</i> , 2001, 344:68 (Exhibit 58)
	Kuypers, Frans A. et al., "Detection of Altered Membrane Phospholipid Asymmetry in Subpopulations of Human Red Blood Cells Using Fluorescently Labeled Annexin V," <i>Blood</i> , 1996, 87:1179-87 (Exhibit 59)
	Larsen, Christian P., Presentation of "Costimulation blockade: Progress toward clinical application" at the American Society of Transplantation Meeting in Las Croabas, Puerto Rico, Jan. 13-17, 2000 (Exhibit 60)
	Larsen, Christian P., Presentation of "Costimulation blockade: progress toward clinical application" at Canadian Society of Transplantation Annual Scientific meeting in Mont Tremblant, Quebec, Canada, March 3-4, 2000 (Exhibit 61)
	Larsen, Christian P. et al., Abstract of "Prolongation of Renal Allograft Survival with Blockade of the CD28 Pathway Using A Novel Mutant CTLA4-IG Fusion Protein In Non-Human Primates," in <i>Transplantation</i> , 2000, 69:S123, #45 (Exhibit 62)
	Larsen, Christian P. et al., Presentation of "Prolongation of Renal Allograft Survival With Blockade of the CD28 Pathway Using A Novel Mutant CTLA4-Ig Protein In Nonhuman Primates" at the American Society of Transplantation Meeting in Chicago, Illinois, March 3-4, 2000 (Exhibit 63)
	Larsen, Christian P., Presentation of "Manipulation of Costimulatory Pathways: Targeting CD80 and CD86" at the XVII congress of the Transplantation Society in Rome, Italy, Aug. 27-Sept. 1, 2000 (Exhibit 64)
	Lasky, Laurence A. et al., "Neutralization of the AIDS Retrovirus by Antibodies to a Recombinant Envelope Glycoprotein," <i>Science</i> , 1986, 233:209-12 (Exhibit 65)


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IN AN APPLICATION

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Lenz, Laurel L. et al., "Requirements for Bone Marrow-derived Antigen-presenting Cells in Priming Cytotoxic T Cell Responses to Intracellular Pathogens," <i>Journal of Experimental Medicine</i> , 2000, 192:1135-42 (Exhibit 66)
		Linsley, Peter S. et al., "Coexpression and Functional Cooperation of CTLA-4 and CD28 on Activated T Lymphocytes," <i>Journal of Experimental Medicine</i> , 1992, 176:1595-604 (Exhibit 67)
		Linsley, Peter S. et al., "Human B7-1 (CD80) and B7-2 (CD86) Bind with Similar Avidities but Distinct Kinetics to CD28 and CTLA-4 Receptors," <i>Immunity</i> , 1994, 1:793-801 (Exhibit 68)
		Linsley, Peter S. et al., "Binding Stoichiometry of the Cytotoxic T Lymphocyte-associated Molecule-4 (CTLA-4)," <i>Journal of Biological Chemistry</i> , 1995, 270:15417-24 (Exhibit 69)
		Lucarelli, G. et al., "Marrow Transplantation for Thalassemia after Treatment with Busulfan and Cyclophosphamide," <i>Annals New York Academy of Sciences</i> , 1985, 445:428-31 (Exhibit 70)
		Lyons, A. Bruce and Christopher R. Parish, "Determination of lymphocyte division by flow cytometry," <i>Journal of Immunological Methods</i> , 1994, 171:131-7 (Exhibit 71)
		Maini, Ravinder et al., "Infliximab (chimeric anti-tumour necrosis factor α monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomized phase III trial," <i>The Lancet</i> , 1999, 354:1932-9 (Exhibit 72)
		Malik, Najma et al., "Molecular Cloning, Sequence Analysis, and Functional Expression of a Novel Growth Regulator, Oncostatin M," <i>Molecular and Cellular Biology</i> , 1989, 9:2847-53 (Exhibit 73)
		Markees, Thomas G. et al., "Long-Term Survival of Skin Allografts Induced by Donor Splenocytes and Anti-CD154 Antibody in Thymectomized Mice Requires CD4 ⁺ T Cells, Interferon- γ , and CTLA4," <i>Journal of Clinical Investigation</i> , 1998, 101:2446-55 (Exhibit 74)
		Martin, Paul J. et al., "Preincubation of Donor Bone Marrow Cells with a Combination of Murine Monoclonal Anti-T-Cell Antibodies Without Complement Does Not Prevent Graft-Versus-Host Disease After Allogeneic Marrow Transplantation," <i>Journal of Clinical Immunology</i> , 1984, 4:18-22 (Exhibit 75)
		Mathiesen, T. et al., "Prolonged survival and vascularization of xenografted human glioblastoma cells in the central nervous system of Cyclosporine A treated rats," <i>Cancer Letters</i> , 1989, 44:151-6 (Exhibit 76)
		Mayumi, Hisanori and Robert A. Good, "Long-Lasting Skin Allograft Tolerance in Adult Mice Induced Across Fully Allogeneic (Multimajor H-2 Plus Multiminor Histocompatibility) Antigen Barriers by a Tolerance-Inducing Method Using Cyclophosphamide," <i>Journal of Experimental Medicine</i> , 1989, 169:213-38 (Exhibit 77)
		Mentzer, William C. and Morton J. Cowan, "Bone Marrow Transplantation for β -Thalassemia: The University of California San Francisco Experience," <i>Journal of Pediatric Hematology/Oncology</i> , 2000, 22:598-601 (Exhibit 78)
		Metzler, William J. et al., "Solution structure of human CTLA-4 and delineation of a CD80/CD86 binding site conserved in CD28," <i>Nature Structural Biology</i> , 1997, 4:527-31 (Exhibit 79)
		Moreland, Larry W. et al., "Etanercept Therapy in Rheumatoid Arthritis: A Randomized, Controlled Trial," <i>Annals of Internal Medicine</i> , 1999, 130:478-86 (Exhibit 80)
		Murali-Krishna, Kaja et al., "Counting Antigen-Specific CD8 T Cells: A Reevaluation of Bystander Activation during Viral Infection," <i>Immunity</i> , 1998, 8:177-87 (Exhibit 81)

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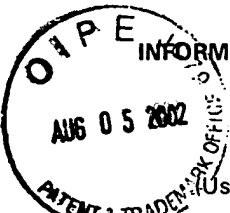
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Murali-Krishna and Rafi Ahmed, "Cutting Edge: Naive T Cells Masquerading as Memory Cells," <i>Journal of Immunology</i> , 2000, 165:1733-7 (Exhibit 82)
	O'Shannessy, Daniel J. et al., "Determination of Rate and Equilibrium Binding Constants for Macromolecular Interactions Using Surface Plasmon Resonance: Use of Nonlinear Least Squares Analysis Methods," <i>Analytical Biochemistry</i> , 1993, 212:457-68 (Exhibit 83)
	Oaks, Martin K. et al., "A Native Soluble Form of CTLA-4," <i>Cellular Immunology</i> , 2000, 201:144-53 (Exhibit 84)
	Owen, Ray D., "Immunogenetic Consequences of Vascular Anastomoses between bovine twins," <i>Science</i> , 1945, 102:400-1 (Exhibit 85)
	Pászty, Chris et al., "Transgenic Knockout Mice with Exclusively Human Sickle Hemoglobin and Sickle Cell Disease," <i>Science</i> , 1997, 278:876-8 (Exhibit 86)
	Peach, Robert J. et al., "Complementarity Determining Region 1 (CDR-1)- and CDR3-analogous Regions in CTLA-4 and CD28 Determine the Binding to B7-1," <i>Journal of Experimental Medicine</i> , 1994, 180:2049-58 (Exhibit 87)
	Pearson, Thomas C. et al., "CTLA4-Ig Plus Bone Marrow Induces Long-Term Allograft Survival and Donor-Specific Unresponsiveness in the Murine Model," <i>Transplantation</i> , 1996, 61:997-1004 (Exhibit 88)
	Pichlmayr, R. et al., "Placebo-controlled study of mycophenolate mofetil combined with cyclosporin and corticosteroids for prevention of acute rejection," <i>The Lancet</i> , 1995, 345:1321-5 (Exhibit 89)
	Platt, Orah S. and Eva C. Guinan, "Bone Marrow Transplantation in Sickle Cell Anemia - The Dilemma of Choice," <i>New England Journal of Medicine</i> , 1996, 335:426-8 (Exhibit 90)
	Ruedl, Christiane et al., "Phenotypic and functional characterization of CD11c ⁺ dendritic cell population in mouse Peyer's patches," <i>European Journal of Immunology</i> , 1996, 26:1801-6 (Exhibit 91)
	Salomon, Benoît and Jeffrey A. Bluestone, "Complexities of CD28/B7: CTLA-4 Costimulatory Pathways in Autoimmunity and Transplantation," <i>Annual Review of Immunology</i> , 2001, 19:225-52 (Exhibit 92)
	Santos, G. W. et al., "HLA-Identical Marrow Transplants in Aplastic Anemia, Acute Leukemia, and Lymphosarcoma Employing Cyclophosphamide," <i>Human Bone Marrow Transplantation</i> , 1976, 63-9 (Exhibit 93)
	Sayegh, Mohamed H. et al., "Donor Antigen is Necessary for the Prevention of Chronic Rejection in CTLA4Ig-Treated Murine Cardiac Allograft Recipients," <i>Transplantation</i> , 1997, 64:1646-50 (Exhibit 94)
	Serke, Stefan and Dieter Huhn, "Identification of CD71 (transferring receptor) expressing erythrocytes by multiparameter-flow-cytometry (MP-FCM): correlation to the quantitation of reticulocytes as determined by conventional microscopy and by MP-FCM using a RNA-staining dye," <i>British Journal of Hematology</i> , 1992, 81:432-9 (Exhibit 95)
	Sfikakis, Peter P. et al., "CD28 Expression On T Cell Subsets In Vivo and CD28-Mediated T Cell Response In Vitro in Patients with Rheumatoid Arthritis," <i>Arthritis & Rheumatism</i> , 1995, 38:649-54 (Exhibit 96)

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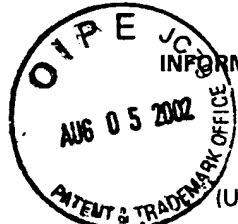
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Shahinian, Arda et al., "Differential T Cell Costimulatory Requirements in CD28-Deficient Mice," <i>Science</i> , 1993, 261:609-12 (Exhibit 97)
	Sharabi, Yedida and David H. Sachs, "Mixed Chimerism and Permanent Specific Transplantation Tolerance Induced by a Nonlethal Preparative Regimen," <i>Journal of Experimental Medicine</i> , 1989, 169:493-502 (Exhibit 98)
	Shehee, W. Ronald et al., "Lethal thalassemia after insertional disruption of the mouse major adult β -globin gene," <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 1993, 90:3177-81 (Exhibit 99)
	Slavin, Shimon et al., "Nonmyeloablative Stem Cell Transplantation and Cell Therapy as an Alternative to Conventional Bone Marrow Transplantation with Lethal Cytoablation for the Treatment of Malignant and Nonmalignant Hematologic Diseases," <i>Blood</i> , 1998, 91:756-63 (Exhibit 100)
	Smith, Douglas H. et al., "Blocking of HIV-1 Infectivity by a Soluble, Secreted Form of the CD4 Antigen," <i>Science</i> , 1987, 238:1704-7 (Exhibit 101)
	Spitzer, Thomas R. et al., "Intentional Induction of Mixed Chimerism and Achievement of Antitumor Responses After Nonmyeloablative Conditioning Therapy and HLA-Matched Donor Bone Marrow Transplantation for Refractory Hematologic Malignancies," <i>Biology of Blood and Marrow Transplantation</i> , 2000, 6:309-20 (Exhibit 102)
	Srinivas, N. R. et al., "Pharmacokinetics and Pharmacodynamics of CTLA4Ig (BMS-188667), a Novel Immunosuppressive Agent, in Monkeys following Multiple Doses," <i>Journal of Pharmaceutical Sciences</i> , 1996, 85:1-4 (Exhibit 103)
	Srinivas, Nuggehally R. et al., "Assessment of Dose Proportionality, Absolute Bioavailability, and Immunogenicity Response of CTLA4Ig (BMS-188667), a Novel Immunosuppressive Agent, Following Subcutaneous and Intravenous Administration to Rats," <i>Pharmaceutical Research</i> , 1997, 14:911-6 (Exhibit 104)
	Swerlick, Robert A. et al., " $\alpha_4\beta_1$ -Integrin Expression on Sickle Reticulocytes: Vascular Cell Adhesion Molecule-1-Dependent Binding to Endothelium," <i>Blood</i> , 1993, 82:1891-9 (Exhibit 105)
	Sykes, Megan et al., "Induction of high levels of allogeneic hematopoietic reconstitution and donor-specific tolerance without myelosuppressive conditioning," <i>Nature Medicine</i> , 1997, 3:783-7 (Exhibit 106)
	Thomas, E. Donnall et al., "Marrow Transplantation for Thalassemia," <i>The Lancet</i> , 1982, 2:227-9 (Exhibit 107)
	Tomita, Yukihiro et al., "Myelosuppressive Condition Is Required to Achieve Engraftment of Pluripotent Stem Cells Contained in Moderate Doses of Syngeneic Bone Marrow," <i>Blood</i> , 1994, 83:939-48 (Exhibit 108)
	Tomita, Yukihiro et al., "Role of Intrathymic Clonal Deletion and Peripheral Anergy in Transplantation Tolerance Induced by Bone Marrow Transplantation in Mice Conditioned with a Nonmyeloablative Regimen," <i>Journal of Immunology</i> , 1994, 153:1087-98 (Exhibit 109)
	Turgeon, Nicole A. et al., "Viral Infection Abrogates CD8 ⁺ T-cell Deletion Induced by Costimulation Blockade," <i>Journal of Surgical Research</i> , 2000, 93:63-9 (Exhibit 110)
	Urlaub, Gail et al., "Effect of Gamma Rays at the Dihydrofolate Reductase Locus: Deletions and Inversions," <i>Somatic Cell and Molecular Genetics</i> , 1986, 12:555-66 (Exhibit 111)

EXAMINER	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.	

*Substitute Disclosure Statement Form (PTO-1449)

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FORM 1449*  IN AN APPLICATION (Use several sheets if necessary)	Docket Number D0136NP/30436.58USU1	Application Number 10/057,288
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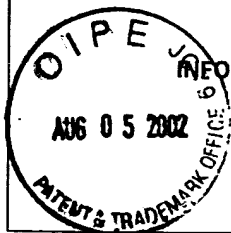
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Vermes, István et al., "A novel assay for apoptosis Flow cytometric detection of phosphatidylserine expression on early apoptotic cells using fluorescein labelled Annexin V," <i>Journal of Immunological Methods</i> , 1995, 184:39-51 (Exhibit 112)
	Vermynen, C. et al., "Haematopoietic stem cell transplantation for sickle cell anaemia: the first 50 patients transplanted in Belgium," <i>Bone Marrow Transplantation</i> , 1998, 22:1-6 (Exhibit 113)
	Walters, Mark C. et al., "Impact of bone marrow transplantation for symptomatic sickle cell disease: an interim report," <i>Blood</i> , 2000, 95:1918-24 (Exhibit 114)
	Warner, G. L. et al., Abstract and Presentation of "Bioactivity of BMS-188667 (CTLA4Ig) in Cynomolgus Monkeys," in Seattle, Washington, March 16-22, 1995 (Exhibit 115)
	Webb, Louise M. C. et al., "Prevention and amelioration of collagen-induced arthritis by blockade of the CD28 co-stimulatory pathway: requirement for both B7-1 and B7-2" <i>European Journal of Immunology</i> , 1996, 26:2320-8 (Exhibit 116)
	Weinblatt, Michael E. et al., "A Trial of Etanercept, A Recombinant Tumor Necrosis Factor Receptor: Fc Fusion Protein, in Patients with Rheumatoid Arthritis Receiving Methotrexate," <i>New England Journal of Medicine</i> , 1999, 340:253-9 (Exhibit 117)
	Weiner, R. et al., Abstract and Presentation of "Validation and PK Application of a Double Antibody Sandwich Enzyme Immunoassay For the Quantitation of Human CTLA4Ig Fusion Protein (BMS-188667) in Mouse Serum," November 6-10, 1994 (Exhibit 118)
	Weiner, Russell et al., Abstract and Presentation of "Validation of an Enzyme Immunoassay for the Quantitation of Human CTLA4Ig Fusion Protein in Human Serum," in Miami, Florida, November 1995 (Exhibit 119)
	Weiner, Russell, Abstract and Presentation of "Automation and Validation of An EIA For Quantitation of Human CTLA4Ig in Monkey Serum," in Miami, Florida, November 1995 (Exhibit 120)
	Weiner, Russell S. et al., "A sensitive enzyme immunoassay for the quantitation of human CTLA4Ig fusion protein in mouse serum: pharmacokinetic application to optimizing cell line selection," <i>Journal of Pharmaceutical and Biomedical Analysis</i> , 1997, 15:571-579 (Exhibit 121)
	Weiner, Russell S., Abstract and Presentation of "Industrial Perspectives of Primary Analytical Tools for Macromolecules- Principles and Applications with Examples" March 1, 2000 (Exhibit 122)
	Wekerle, Thomas et al., "Extrathymic T Cell Deletion and Allogeneic Stem Cell Engraftment Induced with Costimulatory Blockade Is Followed by Central T Cell Tolerance," <i>Journal of Experimental Medicine</i> , 1998, 187:2037-44 (Exhibit 123)
	Wekerle, Thomas et al., "Allogeneic bone marrow transplantation with co-stimulatory blockade induces macrochimerism and tolerance without cytoreductive host treatment," <i>Nature Medicine</i> , 2000, 6:464-9 (Exhibit 124)
	Wells, Andrew D. et al., "Following the Fate of Individual T Cells throughout Activation and Clonal Expansion," <i>Journal of Clinical Investigation</i> , 100:3173-83 (Exhibit 125)
	Welsh, Raymond M. et al., "Virus-Induced Abrogation of Transplantation Tolerance Induced by Donor-Specific Transfusion and Anti-CD154 Antibody," <i>Journal of Virology</i> , 2000, 74:2210-8 (Exhibit 126)
	Whitmire, Jason K. et al., "CD40 Ligand-Deficient Mice Generate a Normal Primary Cytotoxic T-Lymphocyte Response but a Defective Humoral Response to a Viral Infection," <i>Journal of Virology</i> , 1996, 70:8375-81 (Exhibit 127)

EXAMINER	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.	

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Applicant

Christian P. Larsen et al.

Filing Date

January 25, 2002

Group Art Unit

1646

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

Whitmire, Jason K. et al., "CD40-CD40 Ligand Costimulation is Required for Generating Antiviral CD4 T Cell Responses But Is Dispensable for CD8 T Cell Responses," *Journal of Immunology*, 1999, 163:3194-201 (Exhibit 128)

Whitney, J. Barry III, "Simplified Typing of Mouse Hemoglobin (*Hbb*) Phenotypes Using Cystamine," *Biochemical Genetics*, 1978, 16:667-72 (Exhibit 129)

Williams, Matthew A. et al., "Genetic Characterization of Strain Differences in the Ability to Mediate CD40/CD28-Independent Rejection of Skin Allografts," *Journal of Immunology*, 2000, 165:6849-57 (Exhibit 130)

Wood, Brent L. et al., "Increased Erythrocyte Phosphatidylserine Exposure in Sickle Cell Disease: Flow-Cytometric Measurement and Clinical Associations," *Blood*, 1996, 88:1873-80 (Exhibit 131)

Yang, Hyekyung and Raymond M. Welsh, "Induction of Alloreactive Cytotoxic T Cells by Acute Virus Infection of Mice," *Journal of Immunology*, 1986, 136:1186-93 (Exhibit 132)

Yang, Hyekyung et al., "Virus-Induced Polyclonal Cytotoxic T Lymphocyte Stimulation," *Journal of Immunology*, 1989, 142:1710-8 (Exhibit 133)

Yeager, A. M. et al., "Growth retardation and depigmentation of hair after high-dose busulfan and congenic hemtopoietic cell transplantation in mice," *Bone Marrow Transplantation*, 1992, 9:199-204 (Exhibit 134)

Yokochi, Takashi et al, "B Lymphblast Antigen (BB-1) Expressed on Epste.in-Barr Virus-Activated B Cell Blasts, B Lymphoblastoid Cell Lines, And Burkitt's Lymphomas," *Journal of Immunology*, 1982, 128:823-7 (Exhibit 135)

Zarozinski, Christopher C. and Raymond M. Welsh, "Minimal Bystander Activation of CD8 T Cells during the Virus-induced Polyclonal T Cell Response," *Journal of Experimental Medicine*, 1997, 185:1629-39 (Exhibit 136)

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